

## **Systems Biology of Angiogenesis**

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Systems biology approaches to angiogenesis will be presented that include multiscale computational modeling, bioinformatics, and associated in vitro and in vivo experiments. We have developed molecular-level computational models of key angiogenic factors, e.g. hypoxia-inducible factor (HIF), vascular endothelial growth factors (VEGF), and matrix metalloproteinases (MMPs); these are complemented by an agent-based model (ABM) of capillary sprouting and neovascular network formation. The computational approaches to multiscale multi-modular systems modeling will be discussed. Our VEGF model spans the levels from the molecular to whole body and is applied to investigate therapeutic pro-angiogenic interventions in peripheral arterial disease and anti-angiogenic interventions in breast cancer. Our bioinformatic approaches to angiogenesis, aimed at getting a better fundamental understanding of the molecular interactions and at identification of novel therapeutic targets and drug discovery, include protein-protein interaction networks and proteome-wide search for anti-angiogenic motifs.